# Wyeth

**Wyeth Pharmaceuticals**

July 9, 2004

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane,
Room 1061
Rockville, MD 20852

Re: Docket No. 2004N-0133; Electronic Record; Electronic Signatures; Public Meeting; 69 Federal Register 18591; April 8, 2004

Dear Sir/Madam:

The following comments are submitted on behalf of Wyeth Pharmaceuticals. Based on the direction provided in the FDA Part 11 Scope and Application guidance, Wyeth's approach to Part 11 compliance has been modified to focus more on predicate rule record requirements and risk assessments of in-scope systems. Wyeth believes that a risk-based approach is appropriate for the application of Part 11 and encourages incorporation of this approach on a broader scale into the new version of the regulation.

Answers to specific questions posed are provided below.

Sincerely,

Donald J. Sauer
Vice President of Operations
Quality, Regulatory, Safety, Compliance & Audit

*Part 11, Subpart A – General Provisions*

1. We are interested in comments on FDA's interpretation of the narrow scope of Part 11 as discussed in the Part 11 guidance and whether Part 11 should be revised to implement the narrow interpretation described in the guidance.

   Yes, Part 11 should be revised to implement the narrow interpretation described in the guidance. This narrowing provides industry the latitude to implement a wide array of technological and procedural controls while considering system risk in the equation. One size does not fit all and the new interpretation allows for controls to be custom fit to a specific system and situation.

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2. We are interested in comments on whether revisions to definitions in Part 11 would help clarify a narrow approach and suggestions for any such revisions.

The definition of electronic record must be carefully clarified. Definitions associated with the risk management process would also serve to narrow the focus of Part 11 and allow for application of resources in areas of the highest concern.

3. We are interested in comments on the need for clarification in Part 11 regarding which records are required by predicate rules and are therefore required to be Part 11 compliant.

To further clarify and improve the regulation, it is critical that there be a very clear definition of "electronic record" as it relates to part 11. There is a large amount of discussion and confusion around explicit and implicit records required by predicate rules since records that are explicitly required are subject to part 11. We have heard multiple conflicting interpretations from different Agency representatives. Records that are used only to demonstrate compliance with predicate rule requirements fall into a grey area. While we believe that these records should be part of the definition of electronic record, their risk level will dictate the type of controls that are implemented. The definition should also make it clear that draft documents are not regulated records and do not become subject to Part 11control until the first signature is applied or they are released for their intended use (where no signature is required).

*Part 11, Subpart B – Electronic Records*

1. We are interested in comments on whether there are other areas of Part 11 that should incorporate the concept of a risk-based approach, detailed in the Part 11 Guidance (e.g., those that require operational system and device checks).

   Yes, all aspects of Part 11should incorporate a risk-based approach. This shift provides industry the opportunity to examine each system, determine its risk level, and design technological or procedural controls that are appropriate to the level of risk that the system introduces. This also provides the ability to allocate limited resources to the systems that are highest risk and require the most stringent controls to assure data integrity.

2. Is additional clarity needed regarding how predicate rule requirements related to Subpart B can be fulfilled?

   Yes, clarity is needed around which predicate rule requirements are related to Subpart B and how to handle Subpart B items when there are no applicable predicate rules for the activity.

3. Should the requirements for electronic records submitted to FDA be separate from electronic records maintained to satisfy predicate rule requirements?

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No, Part 11 requirements should remain the same for submitted and maintained electronic records. Level of control will be dictated by a risk assessment.

4. Should Part 11continue to differentiate between open systems and closed systems?

   Yes, Part 11should continue to differentiate between open and closed systems. This distinction encourages industry to carefully consider and plan for additional data integrity issues that may be introduced in an open system. Additional controls for open systems are becoming more important as e-commerce increases and other regulatory bodies already mandate such controls.

*Individual Controls in Subpart B*

1. Should the validation provision in Part 11 be retained to ensure that a system meets predicate rule requirements for validation?

   The provision should be modified to allow for the application of a risk-based approach to validation.

2. Are there any related predicate rule requirements that you believe are necessary to preserve, the content and meaning of records with respect to record copying and record retention? What requirements would preserve record security and integrity and ensure that records are suitable for inspection, review, and copying by the agency?

   Copying of electronic records assumes a self-contained record. The meaning for database record is unclear and at times unachievable. Long term record retention and record copying are technically difficult provisions of Part 11and industry should not be expected to retain outdated technology for the sole purpose of providing electronic copies. Part 11 should be revised to incorporate modifications in the guidance that allows for archiving to paper with appropriate procedural controls to reasonable assure authenticity and accuracy.

3. Should audit trail requirements include safeguards designed and implemented to deter, prevent, and document unauthorized record creation, modification, and deletion?

   Yes, audit trail requirements described should be included. However, the approach to audit trails should be risk-based as determined by patient risk posed by the system and impact to public health if there were a problem with record authenticity or integrity.

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4. In light of how technology has developed since Part 11 became effective, should Part 11 be modified to incorporate concepts, such as configuration and document management, for all of a systems software and hardware?

   No, it is not necessary to codify configuration and document management techniques and technologies. A risk-based approach is appropriate for this activity.

*Part 11 Subpart C – Electronic Signatures*

1. Since 11.10(d) does not address the handling of security breaches where an unauthorized individual accesses the system, should Part 11 address investigations and follow up when these security breaches occur?

No additional requirement is necessary.

*Additional Questions for Comment*

1. What are the economic ramifications of modifying Part 11 based on the issues raised in this document?

   Broader and faster implementation of automated technology can improve operational efficiency and reduce product costs to the patient while increasing consistency and compliance and promoting better public health. Resources spent on remediating legacy systems to meet an Agency schedule are not available to implement new systems like PAT.

2. Is there a need to clarify in Part 11 which records are required by predicate rules where those records are not specifically identified in predicate rules? If so, how could this distinction be made?

   Yes. The Agency must define what is meant by "required by predicate rule." The distinction between implicit versus explicit must be clearly delineated.

3. In what ways can Part 11 discourage innovation?

   The timeliness of migrating from older systems to new technology that improves quality, safety, etc. may be slowed due to the costs already incurred to comply with Part 11.

4. What potential changes to Part 11 would encourage innovation and technical advances consistent with the agency's need to safeguard public health?

   Allow industry to develop risk-based justifications for all aspects of the regulation. Remove application of Part 11 to legacy systems. Develop practical expectations regarding long-term record archival, retrieval, and copying.

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5. What risk-based approaches would help to ensure that electronic records have the appropriate levels of integrity and authentic elements and that electronic signatures are legally binding and authentic?

   Judicious and limited application of audit trails to e-signature and to higher risk records only. Risk-based approaches should be direct, easy to use, and efficient to implement.

6. What are stakeholder concerns in regards to modifications made to legacy systems in use as of August 1997?

   Risk mitigation is appropriate to help focus limited resources. A risk-based approach should be applied to legacy systems regardless of when modifications were made and appropriate controls should be implemented based on results of the risk justification.

7. Should Part 11 address record conversion?

   Record conversion should be identified as an acceptable means of maintenance, but this should not be prescriptive.

8. Are there provisions of Part 11 that should be augmented, modified, or deleted as a result of new technologies that have become available since Part 11 was issued?

   Manual signatures and dates applied to hybrid electronic records should not require recording of time.